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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,202	11/05/2001	Stefan Grimm	RDIDO01046US	7800

6449 7590 02/12/2003

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EXAMINER
NGUYEN, QUANG

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 02/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/890,202	GRIMM ET AL.	
	Examiner	Art Unit	
	Quang Nguyen, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants' preliminary amendment filed on 7/26/01 in Paper No. 7 has been entered.

Claims 1-16 are pending in the present application, and they are examined on the merits herein.

Information Disclosure Statement

The information disclosure statement filed on 11/5/2001 in Paper No. 5 has not been considered by the Examiner because the information (PCT documents and a German Office Action) referred to therein is in German, and no translation has been provided for any of the documents. Should Applicants wish the Examiner to consider the disclosed information on the merits, translated documents are required.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. Examiner notes that a translated copy of the priority document has not been provided. Accordingly, the pending claims have the priority date of 01/26/2000.

Claim Objections

Claim 10 is objected to because of the following informalities: the phrase "with reduced endotoxin content obtainable according to a method" is not grammatically

correct. The term - - obtained - - should be used instead of "obtainable". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9 and 11-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1 and its dependent claims, it is unclear what is encompassed by the phrase "removal of protein components and other insoluble components with the fraction not containing said protein and insoluble components being a residue". Do Applicants intend to remove protein components and other insoluble components separately from the fraction not containing the protein components and insoluble components or not? As written, it appears that the there is no separate removal of the two distinct fractions required. Therefore, the next step in the claimed method is the addition of an aqueous solution of potassium acetate to the residue with or without the fraction not containing the protein and insoluble components? Clarification is requested because the metes and bounds of the claims are not clearly determined.

Additionally, claim 1 recites the limitation "from the soluble fraction" in the last step of the claimed method. There is insufficient antecedent basis for this limitation in the claim. Which soluble fraction is referred to? Immediate prior to this step, the

supernatant is incubated with a silica gel-like support material. Clarification is requested because the metes and bounds of the claim are not clearly determined.

In claims 1, 6-7, 13 and 14, it is unclear what is encompassed by the term " silica gel-like". Since the term is not defined in the instant specification, it is unclear what would constitute as a silica gel-like support material or not. Therefore, the metes and bounds of the claims are not clearly determined.

In claim 4, it is unclear what is encompassed by the phrase "is used" on line 2 of the claim. To do what? The metes and bounds of the claim are not clearly determined.

In claim 7, the phrase "the silica gel-like support material is washed at least once with acetone" is unclear. Is the material washed with acetone prior or after the contacting and incubating with the supernatant? Clarification is requested because the metes and bounds of the claim are not clearly determined.

In claim 11, the phrase "A method of using" is unclear, and it renders the claim indefinite. This is because it is unclear what the claimed method is used for. Is it used for transfection? The metes and bounds of the claim are not clearly determined since one can not tell what the method is used for.

Similarly, in claim 12 it is unclear what is encompassed by the phrase "A method of using". One can not tell exactly what this method is used for. Additionally, it is unclear what is meant by the limitation "producing an agent", particularly with respect to the nucleic acids and/or oligonucleotides. The metes and bounds of the claim are not clearly determined.

In claim 13 and its dependent claims, it is unclear what is encompassed by the phrase "detergent/alcohol". Does it mean a solution containing detergent and alcohol or a solution containing either detergent or alcohol? The metes and bounds of the claims are not clearly determined.

In claim 16, the term "and/or" is recited multiple times with terms having overlapping meanings, and it renders confusion to the claim. Therefore, metes and bounds of the claim are also not clearly determined.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 10-12 and 16 is rejected under 35 U.S.C. 102(b) as being anticipated by Horn et al. (Human gene therapy 6:565-573, 1995).

Horn et al. disclose a method for the production of highly purified eukaryotic plasmid expression vector VCL-1005 coding for the production of the HLA-B7 protein, for *in vivo* gene therapy (see abstract and overview summary). The method includes the step of mixing a prepurified biological sample lysate with potassium acetate (see page 567, col. 1 under the section "Lysis and plasmid recovery"). The pharmaceutical-grade plasmid DNA has trace levels of contaminating *E.Coli* DNA and endotoxin (less than 0.03 endotoxin units/ug plasmid DNA), and it is indistinguishable from a nucleic acid with reduced endotoxin content obtained by the method of the present invention. Horn et al. further teach that the highly purified plasmid to be complexed with a cationic lipid and injected directly into established tumors of patients who have been determined to be HLA-B7 negative (page 566, col. 1, bottom of last full paragraph).

Accordingly, Horn et al. anticipate the instant claims.

Claims 10 and 16 is rejected under 35 U.S.C. 102(b) as being anticipated by Levison et al. (J. Chromatography 827:337-344, 1998; Cited in the International Search Report) or Prazeres et al. (J. Chromatography 806:31-45, 1998; Cited in the International Search Report).

Levison et al. teach a method for isolation of plasmid DNA and genomic DNA from bacterial cells an human whole blood by ion-exchange chromatography, wherein the method also includes the step of mixing a prepurified biological sample lysate with potassium acetate (see abstract and page 338, col. 2, second paragraph under the

section "Plasmid DNA isolation"). Levison et al. further teach that additional steps such as size-exclusion chromatography and/or affinity chromatography can be used to reduce endotoxin from the DNA samples (see page 343, col. 2, bottom of first full paragraph).

Prazeres et al. teach a method for preparative purification of supercoiled plasmid DNA using anion-exchange chromatography containing the step of mixing a prepurified biological sample lysate with potassium acetate (see abstract and page 33, col. 2 under the section "Lysis and primary plasmid isolation"). Prazeres et al. further teach that the supercoiled plasmid DNA sample could be further subjected to a gel filtration step, for instance with Sephacryl S1000, to reduce contaminant endotoxins (see page 43, col. 2, the full paragraph).

The purified DNA samples resulted from the teachings of Levison et al. and Prazeres et al. would have reduced endotoxin content similar to the nucleic acid or oligonucleotide sample obtained by the method of the present invention.

Accordingly, the teachings of Levison et al. and Prazeres et al. meet all the limitation of the instant claim.

Therefore, both Levison et al. and Prazeres et al. anticipate the instant claims.

Claims 10-12 and 16 are rejected under 35 U.S.C. 102(e) as being anticipated by Colpan et al. (U.S. Patent No. 6,297,371).

Colpan et al. disclose a process for the isolation and purification of nucleic acids and/or oligonucleotides for use in gene therapy, wherein said process includes the step

of mixing a prepurified biological sample lysate with potassium acetate (see example 1 starting at col. 8), as well as a step of removing endotoxins from the nucleic acids and/or oligonucleotides (see abstract). Colpan et al. further teach that the purified nucleic acids and/or oligonucleotides are suited for use in gene therapy (e.g., cystic fibrosis or muscular dystrophy) as well as genetic vaccination methods (see col. 7, lines 33-48 as well as col. 1, lines 20-32).

Since the purified nucleic acids and/or oligonucleotides with endotoxins being removed taught by Colpan et al. are indistinguishable from nucleic acids and/or oligonucleotides with reduced endotoxin content obtained by the method of the present invention, and the methods of using the same have the same steps, Colpan et al. anticipate the instant claims.

Claims 10-11 and 16 are rejected under 35 U.S.C. 102(e) as being anticipated by Smith et al. (U.S. Patent No. 6,194,562).

Smith et al. disclose a novel method for removing endotoxins from nucleic acids, wherein the method also includes the step of mixing a prepurified biological sample lysate with potassium acetate (see example 1 starting at col. 12). Smith et al. further teach the purified nucleic acids free of endotoxins can be used in a variety of biological applications including transfection of cultured cells and *in vivo* administration of the nucleic acids to organisms which are susceptible to sepsis (see col. 3, lines 15-24).

Since the purified nucleic acids free of endotoxins of Smith et al. are indistinguishable from a nucleic acid with reduced endotoxin content obtained by the

method of the present invention, and the method of using the same has the same steps,

Smith et al. anticipate the instant claims.

Conclusions

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (703) 308-8339.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gerald Leffers, Jr., Ph.D., may be reached at (703) 305-6232, or SPE, Remy Yucel, Ph.D., at (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to LIE, Zeta Adams, whose telephone number is (703) 305-3291.

Quang Nguyen, Ph.D.

Gerald A. Leffers Jr.
PATENT EXAMINER
Gerald C. Leffers Jr
A.U. 1636